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(54) Title: PEPTIDES DERIVATIVES COMPRISING THIAZEPINE GROUP FOR THE TREATMENT OF HYPERLIPIDEMIC CONDITIONS

(57) Abstract: The present invention relates to compounds of formula (I): (wherein variable groups are as defined within) pharmaceutically acceptable salts, solvates, solvates of such salts and prodrugs thereof and their use as ileal bile acid transport (IBAT) inhibitors for the treatment of hyperlipidaemia. Processes for their manufacture and pharmaceutical compositions containing them are also described.

Interna Application No PCT/GB 03/02499

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 CO7K5/065 A61K A61K38/05 A61P3/06 A61P9/10 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) C07K A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ° Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X WO 01 66533 A (ASTRAZENECA UK LTD 1 - 21;DAHLSTROM MICHAEL (SE); ASTRAZENECA AB (SE); B) 13 September 2001 (2001-09-13) method 37 on page 53 page 2, line 5 - line 8; claims; examples 11,34 P,X WO 02 50051 A (ASTRAZENECA UK LTD 1-21 ;ASTRAZENECA AB (SE); BLOMBERG DAVID (SE); STAR) 27 June 2002 (2002-06-27) page 2, line 5 - line 20; claims; examples 83-87, 108, 111-113 Ε WO 03 061663 A (ASTRAZENECA UK LTD 1-21 ;LINDQVIST ANN-MARGRET (SE); ASTRAZENECA AB (SE) 31 July 2003 (2003-07-31) claim 14 Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the 'A' document defining the general state of the art which is not considered to be of particular relevance earfler document but published on or after the International *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-ments, such combination being obvious to a person skilled in the art. document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed *& document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 3 November 2003 10/11/2003 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax: (+31-70) 340-3016 Fuhr, C

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

The scope of claims 1-20, in as far as the expression prodrug is concerned, is so unclear (Article 6 PCT) that a meaningful International Searchis impossible with regard to this expression.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.



pplication No.

Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Although claims 12 and 13 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210 Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet) This international Searching Authority found multiple inventions in this international application, as follows: As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.



Interns Application No PCT /GB03/02499

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0166533	A	13-09-2001	AU	3755601 A	17-09-2001
			BR	0109011 A	03-06-2003
			CA	2401055 A1	13-09-2001
			CN	1416425 T	07-05-2003
			EP	1263747 A1	11-12-2002
			WO	0166533 A1	13-09-2001
			JP	2003525933 T	02-09-2003
			NO	20024217 A	09-10-2002
			US	2003166927 A1	04-09-2003
WO 0250051	A	27-06-2002	AU	2222802 A	01-07-2002
			CA	2431461 A1	27-06-2002
			CZ	20031717 A3	17-09-2003
			EE	200300307 A	15-10-2003
			EΡ	1345918 A1	24-09-2003
			WO	0250051 A1	27-06-2002
			NO	20032829 A	15-08-2003
WO 03061663	Α	31-07-2003	WO	03061663 A1	31-07-2003